
Improving Description of Hydrogen Bonds at the Semiempirical Level: Water–Water Interactions as Test Case

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ABSTRACT: Hydrogen bonding is not well described by available semiempirical theories. This is an important restriction because hydrogen bonds represent a key feature in many chemical and biochemical processes, besides being responsible for the singular properties of water. In this study, we describe a possible solution to this problem. The basic idea is to replace the nonphysical gaussian correction functions (GCF) appearing in the core–core repulsion terms of most MNDO-based semiempirical methods by a simple function exhibiting the correct physical behavior in the whole range of intermolecular separation distances. The parameterized interaction function (PIF) is the sum of atom-pair contributions, each one having five adjustable parameters. In this work, the approach is used to study water–water interactions. The parameters are optimized to reproduce a reference *ab initio* intermolecular energy surface for the water–water dimer obtained at the MP2/aug-cc-pVQZ level. OO, OH, and HH parameters are reported for the PM3 method. The results of PM3-PIF calculations remarkably improve qualitatively and quantitatively those obtained at the standard PM3 level, both for water–dimer properties and for water clusters up to the hexamer. For example, the root-mean-square deviation of the PM3-PIF interaction energies, with respect to *ab initio* values obtained using 700 points of the water dimer surface, is only 0.47 kcal/mol. This value is much smaller than that obtained using the standard PM3 method (4.2 kcal/mol). The PM3-PIF water dimer energy minimum (−5.0 kcal/mol) is also much closer to *ab initio* data (−5.0 ± 0.01 kcal/mol) than PM3 (−3.50 kcal/mol). The method is therefore promising for the development of new semiempirical approaches as well as for application of combined quantum mechanics and molecular mechanics

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Introduction

Hydrogen bonds are clearly the most intriguing and studied type of intermolecular interaction. Their complex and elusive nature, and the crucial role they play in biological systems have intrigued scientists for many years. An accurate description of such weak bonds represents, even today, a great challenge for theoretical chemistry. However, in recent years, rapid evolution of computational capabilities has permitted investigation of simple systems at very high levels of theory, resulting in very good agreement with the most refined experimental data. Large systems have also been investigated, but due to the prohibitive cost of *ab initio* calculations, in such cases, semiempirical methods have been employed more often. Moreover, semiempirical models may be coupled with molecular mechanics approaches¹ to deal, for instance, with proteins or other species containing hundreds or thousands of atoms.

Unfortunately, semiempirical methods do not describe intermolecular interactions that well. The most popular models have been derived from the MNDO² approach, which cannot describe hydrogen-bonded complexes, because of its propensity to overestimate repulsion between atoms at separation distances close to the sum of their van der Waals radii. Much effort has been put forth to overcome this problem and different models, particularly MNDO/H,³ MNDO/M,⁴ AM1,⁵ and PM3,⁶ can in part correct the original MNDO deficiencies. All of these have proposed a modification of the nuclear–nuclear repulsion term. Because this term is outside the quantum-mechanical framework it allows testing of different empirical functions, parameterizing them to reproduce some experimental heats of formation of small hydrogen-bonded complexes. In all cases, a correction term consisting of a gaussian, or a sum of gaussian functions providing an extra stabilizing contribution at the equilibrium distance, is added. MNDO/H is based on the MNDO method and the gaussian core function (GCF) has only been added for hydrogen-bonded atom pairs. In MNDO/M, GCFs are used for in-

teractions between both bonded and nonbonded atoms, while still keeping the whole MNDO parameterization. Conversely, AM1 and PM3, although based on the MNDO approach, have been fully reparameterized. The core–core term of the interaction between atoms *A* and *B* is obtained as follows:

$$E_{AB}^{core} = Z_A Z_B \langle S_A S_A | S_B S_B \rangle (1 + e^{-\alpha_A R_{AB}} + e^{-\alpha_B R_{AB}}) + g(A, B) \quad (1)$$

where Z_A is the core charge, R_{AB} is the internuclear distance, and α_A an atomic parameter. For the case, *A* = oxygen or nitrogen, and *B* = hydrogen, the leading exponential term is multiplied by R_{AH} (angstroms). Also, $g(A, B)$ involves a sum of atomic GCF terms:

$$g(A, B) = \frac{Z_A Z_B}{R_{AB}} \left(\sum_i K_{A,i} e^{-L_{A,i}(R_{AB}-M_{A,i})^2} + \sum_j K_{B,j} e^{-L_{B,j}(R_{AB}-M_{B,j})^2} \right) \quad (2)$$

In this expression, K_i , L_i , and M_i are adjustable parameters that modulate the intensity, steepness, and displacement, respectively, of the gaussian term.

Despite of the noticeable improvement provided by AM1 and PM3 over MNDO results for hydrogen bonds, several works^{7–10} have pointed out some serious weaknesses with these methods. For instance, Csonka and Ángyán^{10b} showed that the GCF for hydrogen has an artificial minimum at 1.8 Å that leads to an inaccurate description of hydrogen-bonded systems. All these investigations proved that: (1) the use of GCFs in the core–core repulsion interactions is not sufficient to ensure a good estimation of the intermolecular interaction energy; and (2) the use of GCFs introduces spurious artifacts into the potential energy surface. The limitations of the GCFs were already pointed out in Dewar's original AM1 study,⁵ where the choice of GCFs was described as a "brute force" approach. Clearly, the development of a new generation of semiempirical methods adapted to intermolecular interactions requires changing the GCFs using other well-behaved functions. Such an ambitious goal still deserves much work and different strategies need to be explored and tested prior to their implementation.

In this article, a modified PM3 parameterization that allows for reproduction of the intermolecular potential energy surface (IPES) for a fundamental system, the water dimer, is developed. As it will be shown, this method leads to an accurate description of H-bonding in water clusters. The proposed methodology may be extended without difficulty to reproduce the IPES of other interacting molecules and is intended to be applicable to any semiempirical method. We suggest a way to develop a new semiempirical approximation based on the present approach that will be explored elsewhere. The principles of the method are presented. We apply them to describe hydrogen bonds in the water dimer and several water clusters. Comparison is made with the standard PM3 results and with available *ab initio* and experimental values reported in the literature.

Principles of the Method

We have chosen to treat the case of water–water interactions because of the fundamental importance of hydration effects in many chemical and biochemical problems. It is well known that AM1 or PM3 predict neither the water dimer interaction energy nor its structure accurately. Thus, our aim is to change the original parameterization of the method so that the following requirements are fulfilled: (1) the potential energy of the monomer is unaffected by the modification; (2) the intermolecular potential energy displays a correct shape over the whole range of intermolecular distances, not only in the equilibrium region; and (3) the computational cost of the method must not be increased. On account of this, several strategies may be envisaged but for the moment the most convenient procedure was found to be:

- Standard PM3 treatment of the electronic contribution to the total energy.
- Standard PM3 treatment of the intramolecular terms of the nuclear repulsion energy.
- Substitution of the GCF for the intermolecular terms by a parameterizable interaction function in the nuclear repulsion energy.

This parameterizable interaction function (PIF) must have a correct physical behavior over the whole range of distances and must be flexible enough to reproduce *ab initio* data for the IPES.

PARAMETERIZABLE INTERACTION FUNCTION

The PIF proposed here is a sum of atom–atom contributions similar to those used in molecular mechanics models. After several tests, the following function was found to give excellent results:

$$PIF = \sum_{A,B}^{inter} g(A,B) = \sum_{A,B}^{inter} \alpha_{AB} e^{-\beta_{AB} R_{AB}} + \frac{\chi_{AB}}{R_{AB}^6} + \frac{\delta_{AB}}{R_{AB}^8} + \frac{\varepsilon_{AB}}{R_{AB}^{10}} \quad (3)$$

where α_{AB} , β_{AB} , χ_{AB} , δ_{AB} , and ε_{AB} are adjustable parameters depending on (A,B) atom types (OO, OH, or HH). Each $g(A,B)$ replaces the corresponding GCF for the (A,B) intermolecular pair in the AM1 or PM3 nuclear repulsion function. It should be pointed out that, in the PIF, there are five parameters for each atom pair. Hence, the total number of adjustable parameters for the water dimer (15) might be compared with the PM3 parameters for the GCF in water (12). We must also emphasize that the PIF has an acceptable physical form: the exponential term is related to short-range repulsion, whereas the remaining terms may be essentially related to electrostatic + induction + dispersion corrections to the semiempirical intermolecular energy. However, in the present context, the PIF is merely an auxiliary function necessary to fit the *ab initio* IPES, so a formal interpretation of the optimized coefficients should not be attempted. It should also be pointed out that the idea of using *ab initio* results for parameterizing molecular interactions has been successfully applied for several molecular models, from molecular mechanics force fields¹¹ to some refined models used in numerical simulations of water and aqueous systems.^{12–15}

PARAMETERS FOR WATER–WATER INTERACTIONS THROUGH PM3

The *ab initio* data used to fit the water–water IPES are based on the work of Saint Martin et al.,¹⁶ who obtained a highly refined potential energy surface of the water dimer that includes structures coming from numerical simulations of liquid water. The monomers have the experimental geometry. Saint Martin et al. used the aug-cc-pVQZ basis set (without g functions)^{17,18} representing 156 functions per water molecule. The correlation energy was computed at the MP2 level. The basis set superposition error (BSSE) has not been accounted for because it is assumed to be small. For example, near the interaction energy minimum, Halkier et al.¹⁹ recently reported a 0.19-kcal/mol correction (3.8%).

TABLE I.
Optimized Parameters for PIF.^a

A, B	$\alpha_{A,B}$	$\beta_{A,B}$	$\chi_{A,B}$	$\delta_{A,B}$	$\varepsilon_{A,B}$
O—O	12.45958	2.502734	−266.2244	12587.53	−89486.91
O—H	49.36554	2.276467	−38.2875	−145.05	651.82
H—H	0.51979	2.489980	50.1011	−676.32	2711.77

^a All parameters in hartrees and bohr.

The parameters in the PIF were optimized to fit the *ab initio* IPES consisting of 700 water–water configurations. In Table I, we present the optimized parameters, and in Figure 1 a comparison of the PIF

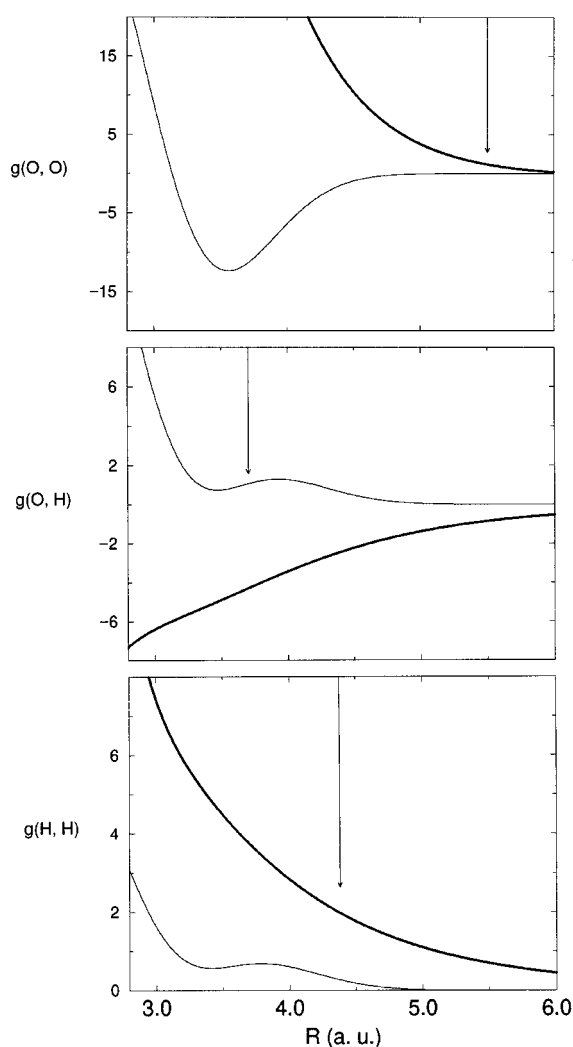


FIGURE 1. Energy contribution (in kcal/mol) for the PM3 GCFs (thin lines) and the PIFs (thick lines) for the three intermolecular atomic pairs in water. Arrows are placed at distances corresponding to those found in the equilibrium geometry of the linear H-bonded water dimer.

functions with the GCF terms they replace. It must be pointed out that, as expected, all the α_{AB} coefficients are positive (short-range repulsion) whereas χ_{AB} , δ_{AB} , and ε_{AB} may be either negative (stabilizing) or positive (destabilizing). Interestingly, the comparison of GCFs and PIF shows that not only the latter have a smoother shape, but also, in the H-bond region, the O—O and O—H contributions are of a different sign.

Results for Water Clusters

The PM3-PIF parameters were incorporated in CHIMISTE/MM.²⁰ This program was then used to test the performance of the parameterization in reproducing selected geometries of small water clusters. It is important to keep in mind that, because no intramolecular parameters were modified, the water monomer in PM3-PIF corresponds to the PM3 prediction; $R_{OH} = 0.953 \text{ \AA}$ and H—O—H angle of 107° . Thus, the PM3-PIF results for water clusters presented in what follows could undoubtedly be improved by also fitting intramolecular parameters. This could be envisaged as a possible way to refine the model in the future.

WATER DIMER IPES

Figure 2 presents the distribution of interaction energies for the 700 different conformations of the water dimer IPES at *ab initio* MP2/aug-cc-pVQZ, PM3 and PM3-PIF levels. The differences between *ab initio* and PM3 profiles are quite remarkable. MP2 displays ample dispersion of the interaction energies whereas PM3 exhibits sharp distribution with a single maximum near $E_{int} = 0 \text{ kcal/mol}$. The distribution pattern of interaction energies obtained with PM3-PIF is in very good agreement with the *ab initio* data. A complementary analysis can be obtained from the direct comparison of interaction energies predicted with different methods. Figure 3 shows such comparison. Again PM3-PIF correlates well with *ab initio* results. A small

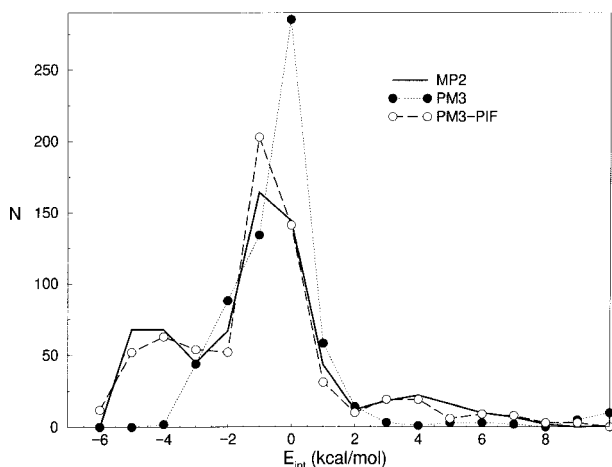


FIGURE 2. Distribution of interaction energies for the 700 water dimer geometries considered in this work.

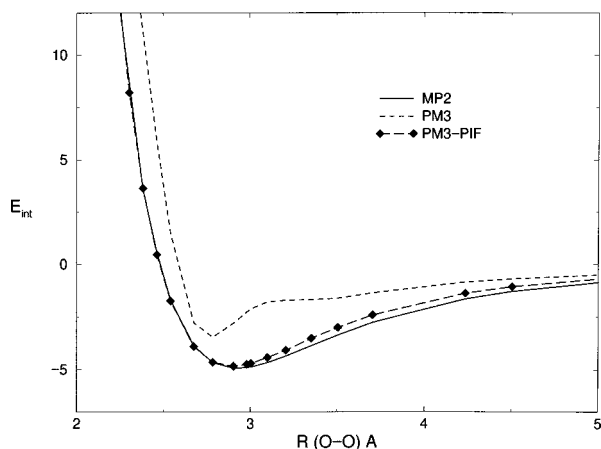


FIGURE 4. Interaction energies (in kcal/mol) for the linear H-bonded water dimer as function of O—O separation. The internal geometries of the monomers correspond to the experimental values.

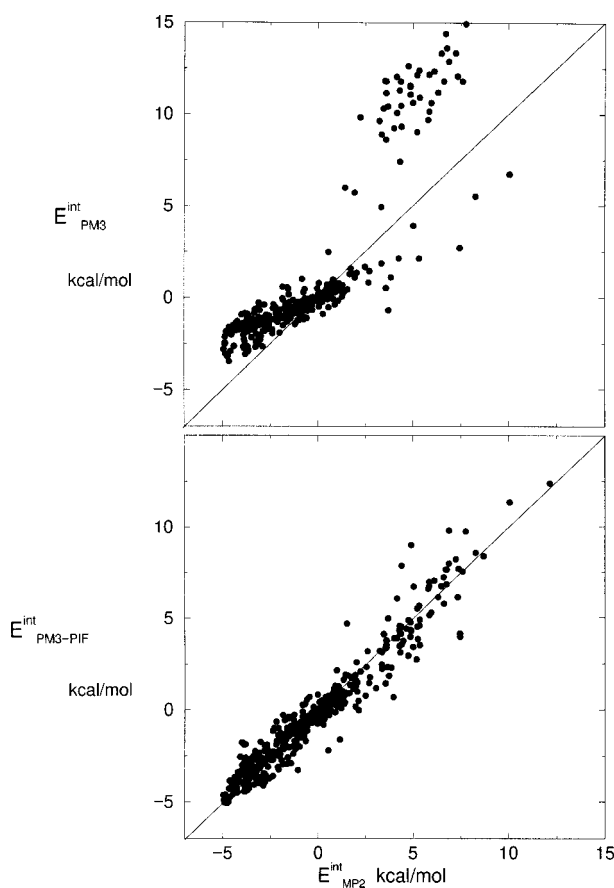


FIGURE 3. Comparison of the interaction energies for the 700 water dimer geometries. The correlation coefficient of the linear fitting is 0.867 for PM3, and 0.981 for PM3-PIF.

root-mean-square deviation (RMSD) is obtained (RMSD = 0.47 kcal/mol) with PM3-PIF, whereas much larger deviations appear with PM3 (RMSD = 4.2 kcal/mol). For comparison, the RMSD obtained with the standard effective pair potential, TIP3P, is intermediate between PM3 and PM3-PIF (RMSD = 2.4 kcal/mol).

The standard PM3, PM3-PIF, and *ab initio* energies for the interaction energy of the linear H-bonded water dimer as a function of the O—O distances appear in Figure 4. One of the most disturbing artifacts produced by the GCF in PM3 appears as an anomalous shoulder at ca. 3 Å. Besides, the position of the minimum for the interaction is very short and the depth of the attractive region very shallow (−3.5 kcal/mol). PM3-PIF does not present the anomalous PM3 behavior and reproduces the *ab initio* results quite well. A detailed comparison of the GCR and PIF functions shows that the latter represent a well-balanced interplay with a more repulsive O—O term (seen in Fig. 1) and a more attractive O—H term that accounts for a proper interaction energy at a reasonable O—O distance.

We now consider the stationary points in the water dimer IPES. This has been thoroughly studied with *ab initio* methods; several studies have been focused on the global minimum^{19, 21–23} and some others in locating the stationary points at the surface.²⁴ The global minimum for the water dimer obtained with PM3-PIF appears in Figure 5. We emphasize that the parameterization was done over a PES where the monomers kept their experimental geometry. The structure in Figure 5 corresponds

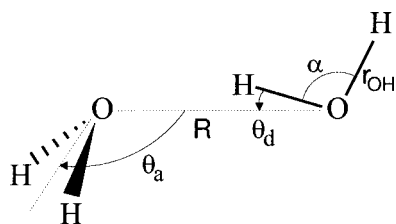


FIGURE 5. The equilibrium structure for the fully optimized PM3-PIF water dimer. $R = 2.846 \text{ \AA}$, $r_{\text{OH}} = 0.956 \text{ \AA}$, and 0.963 \AA for the H-bonded, $\alpha = 107.7^\circ$, $\theta_d = 2.5^\circ$, and $\theta_a = 135.49^\circ$.

to a fully relaxed dimer. The oxygen–oxygen distance is 2.85 \AA . This value is a little shorter than both the best experimental measurement²³ and the most accurate *ab initio* calculation,¹⁹ by 0.10 and 0.05 \AA , respectively. However, it represents a considerable improvement from the 2.7 \AA distance obtained with PM3. The interaction energy for this structure is -5.0 kcal/mol , which is in excellent agreement with both the experimental value of $-5.4 \pm 0.7 \text{ kcal/mol}$,²³ and the benchmark *ab initio* result of $-5.0 \pm 0.1 \text{ kcal/mol}$ recently reported by Halkier et al.¹⁹

Apart from the global minimum, the water dimer IPES exhibits a series of stationary points corresponding to different types of hydrogen bonds; that is, cyclic H bonds, bifurcated structures, etc. In Table II, we present a comparison of the interaction energies obtained with different methods for some of the stationary points on the IPES. In these calculations, we kept the internal geometry of the monomer fixed, for the sake of comparison with results of the work of Smith et al.²⁴ The values in

Table II show that, for most cases, PM3-PIF gives a better approximation of the *ab initio* values than PM3, particularly for structures corresponding to minima characterized in ref. 24. The values also show that both PM3 and PM3-PIF describe very poorly structures corresponding to cyclic structures (4, 5, and 6) in the PES. In particular, PM3-PIF does not improve the PM3 predictions. This is mainly due to an exaggerated H–H repulsion at the very short intermolecular H–H distances characteristic of these dimer arrangements. A few comments are in order. First, one must remember that potential energy surfaces for weakly bound complexes, like the water dimer, usually contain many local minima interconnected by small barriers. Besides, the characterization of stationary points on this surface is very sensitive to the method used. In the case of *ab initio* methods, it is well known that a good description of the outer valence regions is required for a consistent reproduction of the relative energies for these points. In fact, Millot et al.²⁵ showed that most analytical potentials for liquid water are unable to reproduce those structures.

SECOND VIRIAL COEFFICIENT

The second coefficient of the virial expansion for the pressure of a real gas at low density $B(T)$, has been classically assigned to intermolecular pair interactions. In the field of numerical simulations of molecular systems, it has been frequently used as a test of the quality to reproduce a particular analytical potential. As PM3-PIF is a parameterized method, it was of interest to test its performance beyond the IPES used in the fitting procedure. Because

TABLE II. Interaction Energies (kcal/mol) for Some Stationary Points in Water Dimer PES.

Stationary Point ^a	MP2/ aug-cc-pVQZ	Ref. 24	PM3	PM3-PIF
1 Nonplanar C_s	−4.97	−5.40	−3.76	−4.83
2 C_1	−4.02	−4.73	−2.40	−3.29
3 Planar C_s	−4.25	−4.66	−2.51	−4.29
4 Cyclic C_i	−4.08	−4.40	−2.53	−2.44
5 Cyclic C_2	−3.82	−4.08	−2.05	−1.87
6 Planar cyclic C_{2h}	−3.90	−4.03	−1.83	−1.90
7 Triply H-bonded C_s	−2.98	−3.56	−2.20	−2.60
8 Doubly bifurcated C_{2h}	−1.06	−1.65	−1.64	−1.08
9 Bifurcated C_{2v}	−2.99	−3.61	−2.35	−3.30
10 Planar bifurcated C_{2v}	−1.86	−2.56	−2.00	−2.57

^a For all cases we used geometries coming from the Smith et al. work where structures were obtained at the (MP2/6-31+G(d,p)) level and the corresponding (MP4/6-31+G(2d,2p)) energies.²⁴

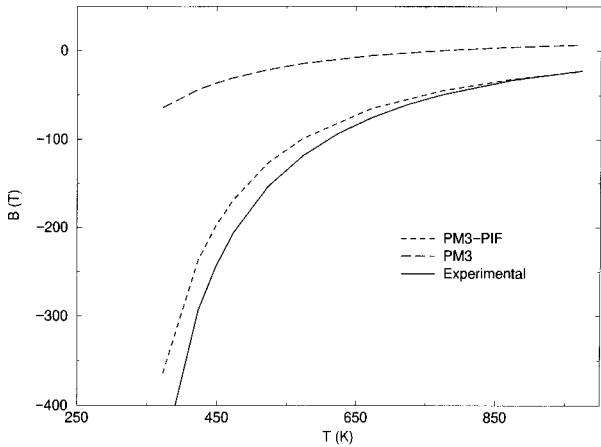


FIGURE 6. Comparison of the second coefficient of the virial obtained for PM3 and PM3-PIF and experimental data from ref. 31.

the calculation of $B(T)$ involves the numerical integration of the Mayer function:

$$f(R) = \langle \exp(-U_{12}(R)/kT) - 1 \rangle_{\omega_1 \omega_2}$$

a random sampling of the PES is required. The R distance between the molecular centers of mass of rigid water molecules in their experimental geometry was varied from 1 to 45 a.u. in steps of 0.075 a.u. For each value, 10,000 orientations were randomly chosen to evaluate the orientationally averaged Mayer function. This procedure allows detecting, in the case of analytical potentials, the ability to reproduce the dimer PES that frequently reflects the quality of the *ab initio* surface used for fitting the corresponding parameters. It is also helpful for detecting any anomalous behavior that may have not previously been seen. A comparison of the experimental values with PM3 and PM3-PIF predictions is shown in Figure 6. A reasonably good agreement is obtained between PM3-PIF and experimental results. It can also be seen that a remarkable improvement over PM3 was achieved.

WATER CLUSTERS: FROM TRIMER TO HEXAMER

Water clusters are useful for approaching the study of liquid water. It is expected that the understanding of their structure and dynamics will shed light in bulk-phase phenomena. Thanks to recent experimental information obtained from the terahertz vibration–rotation–tunneling spectroscopy and results coming from high-level quantum-chemistry computations of small clusters it is possible to have a detailed description of this type of system.

TABLE III. Interaction Energies for Fully Optimized Geometries with PM3 and PM3-PIF and Results Coming from Higher Level Methodologies.

Structure	PM3	PM3-PIF	<i>Ab initio</i>
Dimer	−3.50	−5.03	−5.01 ± 0.1 ^a
Cyclic trimer	−10.08	−12.31	−15.9 ± 0.2 ^b
Cyclic tetramer	−18.36	−23.66	−27.9 ^c
Cyclic pentamer	−23.88	−31.89	−37.7 ^d
Cyclic hexamer	−30.63	−39.82	−42.56 ^e

All terms are in kcal/mol.
^a Ref. 19 CCSD(T) basis set limit.
^b Ref. 26 MP2/aug-cc-pCV5W.
^c Ref. 27 MP2/aug-cc-pVDZ (BSSE uncorrected).
^d Ref. 28 MP2/6-31G(d,p) (BSSE corrected).
^e Ref. 40 MP2/HZ4P(2fg,2d)++ level (BSSE corrected).

We also tested the ability and accuracy of PM3-PIF in reproducing structural and energetic properties of water clusters, from the trimer to the hexamer. In Table III, the binding energies for the cyclic structures are shown and compared with the corresponding PM3 and *ab initio* data. PM3-PIF interaction energies show good agreement with higher level calculations and represent a considerable improvement over PM3 energies. Considering that PM3-PIF was formulated for water dimers, the results are very encouraging, although interaction energies for clusters are systematically smaller than *ab initio* ones. This could be related to an underestimation of cooperative effects. Nonadditive contributions are a known source of stabilization in water clusters^{27, 28, 30–33} and are crucial for understanding the complex interplay between intra- and intermolecular properties. To better understand the origin of the PM3-PIF and MP2 differences, as well as to test the ability of PM3-PIF to predict cooperative effects, we calculated the many-body contributions to the interaction energy for the cyclic clusters.

Many-body terms were calculated within the noncanonical scheme that conduces to convergent results for fully relaxed systems.³³ Relaxation energy of the monomers was included as a zero-order term on the noncanonical expansion scheme. Thus:

$$E_{i,j,\dots,n}^{\text{int}} = \sum V_{ij} + \sum \delta_i + \eta_3 + \dots + \eta_n \quad (4)$$

where δ_i corresponds to the relaxation energy of the monomers calculated as $\delta_i = E_i - E_0$ and the two body terms as $V_{ij} = E_{ij} - (E_i - E_j)$. Larger contributions, for example, the three-body nonadditivities,

TABLE IV.

Decomposition of Interaction Energies for Cyclic Water Clusters under the Noncanonical Scheme (Terms in Parentheses Correspond to Three-Body-Term Percentual Contribution to Total Interaction Energy of Aggregate).

N-body term	Cyclic Trimer	Cyclic Tetramer	Cyclic Pentamer
$\sum \delta_i$	0.37	0.29	1.57
$\sum V_{ij}$	-11.86	-21.54	-28.48
η_3	-0.83 (7%)	-2.92 (12%)	-4.29 (13.5%)
η_4		-0.34	-0.62
η_5			-0.07
Total E_{int}	-12.31	-22.92	-31.89

All terms are in kcal/mol.

are obtained in the usual form as:

$$\eta_3 = E_{ijk}^{\text{int}} - \sum_{ij} V_{ij} - \sum_i \delta_i \quad (5)$$

Results presented in Table IV confirm that PM3-PIF has no size inconsistency because the analysis of the many-body contribution to the interaction energy shows the expected convergence, with the main term coming from the pairwise energy, V_{ij} . However, the computed three- and four-body non-additivities appear to be remarkably smaller than those coming from *ab initio* MP2 studies. For instance, Hodges et al.³² reported that the three-body contributions accounted for 17.2%, 24.6%, and 27.4% of the total interaction energy for the cyclic trimer, tetramer, and pentamer, respectively. To obtain the correct description of cooperative effects, a reparametrization of the monomer might be necessary.

$R(\text{O}—\text{O})$ distances for the water dimer and the cyclic clusters are shown in Figure 7 where a comparison is done with current experimental measurements and high-level theoretical results whenever possible. The predicted trend in contraction of O—O separation, which is a well-known consequence of the cooperative effects, is reasonably well predicted.

Three-dimensional noncyclic structures represent a great challenge for theoretical and experimental methodologies, due in part to a more complex H-bonding pattern. We explored some pentamer and hexamer structures, because they are the most common aggregates appearing in liquid water.³⁶ The geometries of those clusters were fully optimized using PM3-PIF. For the pentamer case, two stable structures, cyclic and cage, were chosen. The former comes to be about 1.8 kcal/mol more stable than the latter from calculations at the MP2-correlated level and with BSSE correction. According to Hodges et al.,³² reproducing this small but significant differ-

ence is not straightforward. PM3-PIF predicts the cyclic structure to be 1.7 kcal/mol more stable than the cage.

The hexamer case deserves special attention. In the past 2 years the structure for $(\text{H}_2\text{O})_6$ has been thoroughly analyzed^{29,36–40} and several low-lying structures have been characterized. The relative stabilities of these structures have not been fully determined, because differences of < 0.5 kcal/mol were found at different levels of theory. In Table V, we present some structural parameters of the lowest lying structures found for water hexamers as well as their interaction energies. We found several close energy structures, *book*, *cycle*, *prism*, and *cage*, that lie 0.08, 0.50, 0.57, and 1.23 kcal/mol above the *bag* hexamer. PM3-PIF does not predict an energy ordering like the one found with a more refined methodology, but predicts, first, a noncyclic structure as the most stable arrangement for the hexamer

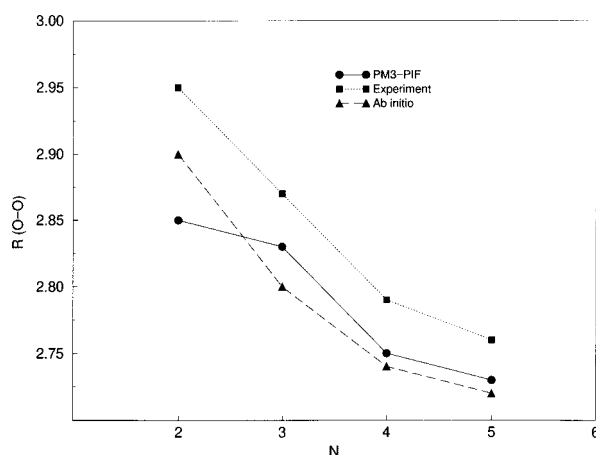


FIGURE 7. O—O distance (in angstroms) as a function of the number of molecules in the cyclic $(\text{H}_2\text{O})_N$ clusters. Experimental data from refs. 34 and 35, and *ab initio* values from refs. 19 and 27.

TABLE V. **Structural Parameters and Interaction Energies for Lowest Lying Water Hexamers. (The H-Bonding Pattern N(*ddaa*) Represents N Number of Molecules with a (*ddaa*) Pattern, *d* for HHH-Bond Donator of a for H-Bond Acceptor.)**

Structure	No. of H bonds	H-Bonding Patterns	<i>R</i> (O—O) ^a	PM3-PIF	<i>Ab initio</i> ^b
(H ₂ O) ₆ (cyclic)	6	6(<i>da</i>)	2.73 ± 0.00	−40.57	−42.56
(H ₂ O) ₆ (book)	7	(<i>dda</i>), (<i>daa</i>), and 4(<i>da</i>)	2.76 ± 0.06	−40.98	−43.32
(H ₂ O) ₆ (bag)	7	(<i>dda</i>), (<i>daa</i>), and 4(<i>da</i>)	2.76 ± 0.06	−41.07	−42.7
(H ₂ O) ₆ (cage)	8	2(<i>dda</i>), 2(<i>daa</i>), and 2(<i>da</i>)	2.80 ± 0.06	−39.82	−43.56
(H ₂ O) ₆ (prism)	9	3(<i>dda</i>) and 3(<i>daa</i>)	2.82 ± 0.07	−40.50	−43.64

^a Average O—O distances are in Å and energies in kcal/mol.
^b Energies from ref. 40.

case and, second, is capable of accounting for the multim minima flat surface in this type of cluster. Both characteristics are important when searching for a realistic description of H bonds.

Conclusions

The parameterizable interaction function (PIF) proposed in this study exhibits some valuable features. It has the correct physical behavior of a function that is intended to fit an intermolecular potential energy surface. It is flexible enough but contains a limited number of adjustable parameters, comparable to that employed in the core–core repulsion function of semiempirical theories. Besides, the additional computational cost is negligible.

The parameterization of such a function may be made in different ways. Here, we have chosen to study water–water interactions, and therefore we have fitted the O—O, O—H, and H—H PIFs to the refined *ab initio* water-dimer IPES. We did not investigate the transferability of these parameters, which was beyond the aim of the present work and will be analyzed in future studies. However, ad hoc parameterization as a function of the chemical species of interest seems feasible. This may require some preliminary computations at the *ab initio* level if the IPES is not known, but has the advantage of leading to a “problem-adapted,” semiempirical approach. The idea may be extended, without difficulty, to energy surfaces for chemical process, as we will show in a forthcoming work.

Finally, a whole replacement of semiempirical GCFs in core–core energy terms by PIFs could be an adequate way to attempt a full reparametrization of methods like AM1 or PM3. The behavior of the core–core terms at short distances should be dominated by the MNDO-type repulsive contributions, whereas at intermediate and long distances, PIF corrections should play a significant role. For this purpose, and to keep the total number of parameters reasonable, the use of atomic quantities instead of pair parameters should be envisaged. Obviously, work is still necessary to assess this possibility, but the results presented in this study are quite encouraging.

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